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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/604,400
Filing Date: July 17, 2003
Appellant(s): KOOL, ERIC T.

J. Wendy Davis
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 21, 2007 appealing from the Office action mailed October 17, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

1) Livak, K.J. et al. "Oligonucleotides with Fluorescent Dyes at Opposite Ends Provide a Quenched Probe System Useful for Detecting PCR Product and Nucleic Acid Hybridization" PCR Meth. Appl., vol. 4, no. 6 (June 1995), pp. 357-362.

2) Xu, Y. et al. "Nonenzymatic Autoloigation in direct three-color detection of RNA and DNA point mutations" Nature Biotechnolo., vol. 19 No. 2 (February 2001), pp. 148-152.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Interpretation

1. Applicant did not define the term "fluorophore compound", therefore it is interpreted as either unimolecular or multimolecular entity.

2. Applicant did not define the term "fluorescence quenching leaving group", therefore it is interpreted as any fluorescence quenching group.

3. Applicant did not define what it means for the fluorescence to be quenched. For example, in the case of a fluorescence donor-acceptor pair, the fluorescence intensity of the donor usually decreases in the presence of the fluorescence acceptor, therefore in this case the acceptor is considered as a fluorescence quencher.

4. The art rejections presented below are based on different interpretation of the meaning of the term "fluorescence quenching leaving group", as explained above.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-8, 10, 11 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Livak et al. (PCR Meth. Appl., vol. 4, pp. 357-362, 1995; cited in the IDS).

Regarding claim 1, Livak et al. teach a nucleic acid probe comprising a fluorophore FAM and a quencher TAMRA (Fig. 1; page 357, second and third paragraphs; page 358, first and last paragraphs; page 360, fourth paragraph).

Regarding claims 2-4, Livak et al. teach quenching efficiency of at least 2-fold (Fig. 2).

Regarding claims 5 and 6, Livak et al. teach nucleic acid probes (Fig. 1; page 357, second and third paragraphs).

Regarding claims 7 and 8, Livak et al. teach both single-stranded and double-stranded nucleic acid probes (Fig. 1; page 357, last paragraph; page 358, first paragraph; Table 1; page 360, second paragraph).

Regarding claim 10, Livak et al. teach the quenching group attached to the internal nucleotides and to the 3'-end of the probe (Fig. 1; Fig. 2).

Regarding claim 11, Livak et al. teach the quenching group attached one nucleotide away from the fluorophore (Fig. 2, probe A1-2).

Regarding claim 14, Livak et al. teach fluorescein and TAMRA (page 357, last paragraph; page 358, first paragraph).

7. Claims 1, 5-7, 9 and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. (Nat. Biotechnol., vol. 19, pp. 148-152, February 2001).

Regarding claim 1, Xu et al. teach a fluorophore compound consisting of two nucleic acid probe pairs, where the 13 bp probe contains a FAM fluorophore and the 7 bp probe contains either a ROX acceptor (= quencher) or a HEX acceptor (= quencher) (fig. 3; page 150, paragraphs 2-5).

Regarding claims 5 and 6, Xu et al. teach nucleic acid probes (Fig. 3).

Regarding claim 7, Xu et al. teach single-stranded probes (Fig. 3).

Regarding claim 9, Xu et al. teach the quenchers attached to the 5' hydroxyl group (Fig. 3; page 151, sixth paragraph).

Regarding claims 12 and 13, Xu et al. teach the compound comprising a nucleophilic phosphorothioate group (Fig. 3; page 151, fifth paragraph).

Regarding claim 14, Xu et al. teach ROX (Fig. 3).

8. No references were found teaching or suggesting claim 15. Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

(10) Response to Argument

Issues in the case

I. Claim Interpretation Issues

A) Regarding the term "fluorophore compound" Appellant argues that it is clear from the description of a compound present, for example, in paragraph [0021], that the claimed compound is a unimolecular entity. However, there is no basis for this restriction of the term's meaning in the disclosure. Appellant did not define the term as a strictly unimolecular entity. Appellant argues that the examples provided in the specification in paragraph [0034] all point to single molecules, and that the Court of Appeals for the Federal Circuit ruled that the specification might define the terms by implication. However, for example, "a protein" does not imply a single molecule, since a large proportion of proteins are multimolecular. Further, the specification does not explicitly exclude the possibility that the compound contains more than one molecule.

Therefore, considering that no specific chemical structure is claimed as the "compound", the originally used interpretation of the term is maintained.

B) Regarding the terms "fluorescence quenching leaving group", "leaving group" and "quenching", Appellant argues that the term "leaving group" is defined in the specification in paragraph [0037] (actually it is paragraph [0035]) as:

"Leaving groups as in general are defined by (a) their ability to activate an atom (to which they are attached) for attack by a nucleophile group and (b) to leave (either simultaneously or subsequently) when the nucleophile does attack".

So what does it mean in terms of the structure of the claimed compound, which is what is being compared here to the prior art? In general, for every chemical bond connecting two chemical groups there is somewhere a nucleophilic group, which will attack it under proper chemical conditions. Further, the above-presented description only requires that the "leaving group" leaves at some point in time (in principle, in might be years later). Therefore, in absence of any particular chemical structure claimed this limitation reads on any fluorescent dye with acceptor properties.

Appellant further argues that the term "quenching" is described through examples in paragraphs [0021], [0033] and in Example 2. Again, Appellant provided no specific definition of the term "quenching group" and no specific structures are claimed. Further, it is well known in the art of fluorescent labeling dyes that acceptor molecules are in fact fluorescence quenchers. For example, here is the description of the process provided by Livak et al. on page 357, first paragraph:

"The fluorogenic probe consists of an oligonucleotide with a reporter fluorescent dye, such as fluorescein, attached to the 5' end; and a quencher dye, such as a rhodamine, attached internally. When the fluorescein is excited by irradiation, its fluorescent emission will be quenched if the rhodamine is close enough to be excited through the process of fluorescence energy transfer (FET).[4,5] During PCR, if the probe is hybridized to a template strand, Taq DNA polymerase will cleave the probe because of its inherent 5' -> 3' nucleolytic activity. If the cleavage occurs between the fluorescein and rhodamine dyes, it causes an increase in fluorescein fluorescence intensity because the fluorescein is no longer quenched." (emphasis added)

Therefore, as can be seen from the above description, should the rhodamine be removed from the probe by any means, the fluorescein emission will increase, thus, functionally, the acceptor rhodamine is a quencher.

Therefore, in view of the above arguments, the term "fluorescent quenching leaving group" is interpreted as any fluorescent acceptor group.

II. Arguments regarding art rejections

A) Regarding the rejection of claims 1-8, 10, 11 and 14 under 35 U.S.C. 102(b) as anticipated by Livak et al., Appelant argues that Livak et al. do not teach fluorescence quenching leaving group or a fluorophore compound comprising a fluorophore group and a florescence quenching leaving group. Appellant argues that rhodamine is not a quenching leaving group as defined in the claimed invention, and that the fluorescein, rather than the rhodamine, leaves the probe under cleavage by the polymerase.

The issues presented were discussed above. Structurally, the fluorophore compound is the oligonucleotide probe of Livak et al. with fluorescein at its 5' end (= fluorophore) and the

rhodamine at different positions within the probe (= quencher). As to whether the rhodamine is a leaving group, as discussed above, under a proper set of chemical conditions with a proper nucleophile it eventually might leave the probe. Therefore, the structure of Livak et al. anticipates then functional terms of the claim language.

The rejection is maintained.

B) Regarding the rejection of claims 1, 5-7, 9 and 12-14 under 35 U.S.C. 102(b) as anticipated by Xu et al., Appellant argues that Xu et al. do not teach a single molecule, but rather two separate probes, and that neither the ROX nor the HEX quencher is a leaving group. The issue of term definitions was addressed above. Again as discussed above, under a proper set of chemical conditions with a proper nucleophile either one of these acceptors eventually might leave the probe.

Therefore, the rejection is maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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